≈> d his (FILE 'HOME' ENTERED AT 15:31:53 ON 08 OCT 2002) FILE 'MEDLINE, CAPLUS, BIOSIS, SCISEARCH' ENTERED AT 15:32:06 ON 08 OCT L1 2255 S REPLICATION (3A) DEFICIENT (4A) ADENOVIR? L213390 S E1A OR E1B L3 80 S L1 AND L2 L4403791 S CYTOKINE OR INTERLEUKINE L5 665117 S CYTOKINE OR INTERLEUKIN 1.6 2 S L3 AND L5 278 S L5 AND L1 L72 DUP REM L6 (0 DUPLICATES REMOVED)  $\Gamma$ 8 L9 186 S L1(S)L5 34 S L1(6A)L5 L10 L11 14 DUP REM L10 (20 DUPLICATES REMOVED) 74 DUP REM L9 (112 DUPLICATES REMOVED) L12=> d bib ab 1-2 18 T.8 ANSWER 1 OF 2 MEDLINE AN 2002118211 MEDLINE DN 21834180 PubMed ID: 11844116 ΤI Infection of replication-deficient adenoviral vector enhances interleukin-8 production in small airway epithelial cells more than in large airway epithelial cells. ΑU Kodama Y; Setoguchi Y; Fukuchi Y Department of Respiratory Medicine, Juntendo University, School of CS Medicine, 2-1-1 Hongo, Bunkyo-Ku, Tokyo 113-8421, Japan. SO RESPIROLOGY, (2001 Dec) 6 (4) 271-9. Journal code: 9616368. ISSN: 1323-7799. CY Australia DTJournal; Article; (JOURNAL ARTICLE) LΑ English FSPriority Journals EM200203 ED Entered STN: 20020221 Last Updated on STN: 20020307 Entered Medline: 20020306 AB OBJECTIVE: In clinical trials or experiments of gene therapy, airway administration of an adenoviral-based vector (E1A-deleted) elicits a dose-dependent inflammatory response with limitation in the duration of transgene expression. The purpose of this study was to evaluate the possibility that the adenoviral-based vector directly enhances IL-8 production independent of adenoviral E1A in normal human airway epithelial cells and to examine the different responses between primary human bronchial epithelial cells (HBE) and primary human small airway epithelial cells (HSAE) in production of IL-8 following exposure to an adenovirus vector. METHODOLOGY: Interleukin (IL)-8 levels were evaluated in the culture medium from HBE and HSAE treated with increasing doses of E1A-deleted adenoviral vector contained the Escherichia coli LacZ reporter gene (AdCMVLacZ). To clarify

the mechanism of enhancing IL-8 production in airway epithelial cells by infection with adenovirus vector, alphavbeta5 agonistic antibody as an analogue of adenoviral capsid and adenoviral capsid vector denatured by exposure to ultraviolet (UV) light were used in the present study.

RESULTS: Inoculation of HBE with AdCMVLacZ at a multiplicity of infection (MOI) of between 1 and 200 resulted in a dose-dependent expression of

LacZ, and maximal expression was observed at a MOI of 100. In contrast, inoculation of HSAE with AdCMVLacZ resulted in maximum expression of LacZ at a MOI of 10. **Interleukin**-8 levels in culture media from the same experiments revealed significantly greater production of IL-8 in

**HSAE** 

PRAI US 1997-978539

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inoculated with AdCMVLacZ at a MOI of 50, compared to HBE under the same conditions. The capsid-denatured adenoviral vector did not enhance IL-8 production, and alphavbeta5 agonistic antibody induced IL-8 enhancement. CONCLUSION: These results suggest that the adenoviral vector directly induces the expression of airway epithelial inflammatory cytokines in the pathogenesis of inflammation and that small airway cells have a greater affinity for adenovirus than other airway epithelial cells.

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    ANSWER 2 OF 2 CAPLUS COPYRIGHT 2002 ACS
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    Construction of modified SV40 viral vectors for gene delivery
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IN
    Board of Regents, the University of Texas System, USA
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     PCT Int. Appl., 84 pp.
     CODEN: PIXXD2
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         RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES,
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             CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
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AB The present invention provides SV40-based viral vectors for use in the delivery of genes to target cells. The unique combination of multiple viral systems provides for vectors with increased carrying capacity and extended host range when compared to normal SV40 vectors. The infectious SV40 viral vector comprises (1) providing an SV40 viral vector comprising an SV40 origin of replication and an expression region operably linked to a first promoter active in eukaryotic cells, wherein said vector lacks SV40 coding sequences; (b) providing a replication-

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deficient adenoviral helper virus having the late region of JC virus or BK virus under the control of a second promoter active in eukaryotic cells; (c) infecting host cells with said adenoviral helper virus; (d) transfecting said host cells with said vector; (e) culturing said host cells for a period of time sufficient to permit said vector to replicate and be packaged; and (f) harvesting said packaged vector in an infectious form. The first and second promoter may be a cytomegalovirus immediate-early or SV40 immediate-early promoter. The host cells may express a polyomavirus large T antigen, for example, like COS-7 cells. The adenoviral helper virus may lack E1 regions. Uses for the vectors include the expression of proteins in vitro and in vivo.

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Centre National de la Recherche Scientifique, Fr.; Cancer Research
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TI Adenovirus-mediated transfer of genes to the gastrointestinal tract
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